

# PATENT ABSTRACTS OF JAPAN

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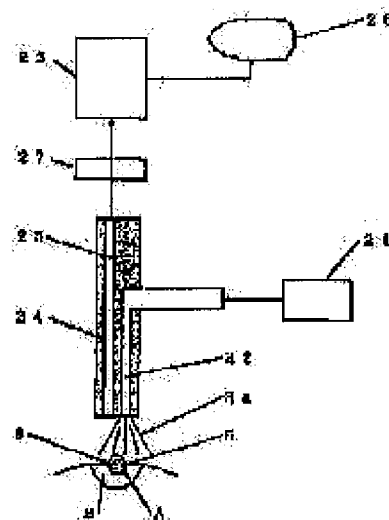
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## (54) MEDICAL DIAGNOSIS AND TREATMENT UNIT

### (57)Abstract:

**PROBLEM TO BE SOLVED:** To provide a medical diagnosis and treatment unit capable of diagnosis while administering treatment by use of a medical laser device working on a single light source both for photochemical diagnosis and treatment and oscillating a wavelength effective for plural types of photosensitive substances and excitation conditions.

**SOLUTION:** A medical diagnosis and treatment unit of this design comprises a medical laser device 21 using a semiconductor laser device as the light source with its half-width value narrow and oscillation wavelength variable, a light transmission line 22 for guiding an irradiation laser beam 3a emitted by the medical laser device 21 toward a focus 5, an image transmission line 23 for the observation of the focus 5 and its vicinity, and a fluorescence isolating means 27 for isolating the fluorescence emitted by the photosensitive substance upon exposure to the



irradiation laser beam 3a. The unit also has an image pickup and analysis means 25 for dealing with the fluorescent image obtained, and an image display means 26 for the exhibition of the result of the analysis.

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## CLAIMS

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### [Claim(s)]

[Claim 1]Diagnosis and a therapeutic device which diagnoses by laser beam which uses focus parts, such as cancer, for a therapy in a device diagnosed and/or treated because a photosensitive substance which has compatibility in a tumor irradiates with light from a light source a focus part made to have accumulated beforehand and excites said photosensitive substance, and a laser beam of an abbreviated identical wavelength.

[Claim 2]Diagnosis and the therapeutic device according to claim 1 which performs a therapy and diagnosis simultaneously.

[Claim 3]any of wavelength of a laser beam used for wavelength of a laser beam used for a therapy, and diagnosis -- although -- diagnosis and the therapeutic device according to claim 1 or 2 in an absorption wavelength band of a photosensitive substance.

[Claim 4]Claim 1 provided with a laser light source single since it irradiates with a laser beam for a therapy, and a laser beam for diagnosis, or diagnosis and a therapeutic device given in 2 or 3.

[Claim 5]Claim 1 characterized by comprising the following, or diagnosis and a therapeutic device given in 2 or 3.

While half breadth of a laser beam for a therapy and a laser beam for diagnosis is narrower than width of an absorption wavelength band chosen at the time of an inner therapy of an absorption wavelength band of a photosensitive substance, they are a laser beam for said therapy, and a laser beam for said diagnosis.

Fluorescence separating mechanism which separates a fluorescence which said photosensitive substance shows.

[Claim 6]An optical transmission line which draws a laser beam near a focus part, and a picture transmission way to which a fluorescence which a photosensitive substance excited by

said laser beam shows is led, Fluorescence separating mechanism which separates only said fluorescence, and image pick-up / analysis means which picturizes and carries out analysis processing of the fluorescence image acquired by said fluorescence separating mechanism, Diagnosis and the therapeutic device according to claim 2 or 3 which is provided with an image display means which displays an analysis processing result of said fluorescence image, and displays said fluorescence image by said image display means also during a therapy of said focus part.

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[Translation done.]

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## DETAILED DESCRIPTION

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### [Detailed Description of the Invention]

[0001]

[Field of the Invention]The photosensitive substance which has compatibility in a tumor irradiates with the light corresponding to the absorption wavelength of the photosensitive substance the focus part of tumors, such as cancer made to have accumulated beforehand, and this invention excites a photosensitive substance, and relates to the diagnosis and the therapeutic device which diagnoses and/or treats a focus part.

[0002]

[Description of the Prior Art]In recent years, the photochemistry diagnosis (it is described as Photodynamic Diagnosis and following PDD) and the photochemistry therapy (it is described as PhotodynamicTherapy and the following PDT) using a laser beam are developing quickly with progress of the electronic iatrotechnique. The photosensitive substance which has photochemical reactions, such as firefly luminescence and a cytocidal action, when it has compatibility in a tumor and is excited by light in this PDD and PDT is made to accumulate on the focus part of tumors, such as cancer, beforehand, By irradiating this focus part, a photosensitive substance is excited and the diagnosis (PDD) of a focus part by measurement of that luminescence fluorescence and the focus part by cytotoxicity reaction are treated (PDT). Since it is better for the wavelength of irradiation light to have agreed in the absorption wavelength of a photosensitive substance in order to excite a photosensitive substance efficiently, the laser light source of the wavelength which suited the absorption wavelength of the photosensitive substance used as a light source of irradiation light is used.

[0003]As diagnosis and a therapeutic device of this kind of cancer, conventionally, . Were indicated by JP,63-2633,B and JP,63-9464,B. The device using the die laser (henceforth excimer die laser) excited using excimer laser as a laser light source is known well, using a hematoporphyrin derivative as a photosensitive substance. It explains referring to drawings for

the diagnosis and the therapeutic device of cancer using the conventional laser device indicated by JP,63-2633,B and JP,63-9464,B hereafter.

[0004]Drawing 4 shows the outline lineblock diagram of the diagnosis and the therapeutic device of cancer using the conventional laser device. A is a cancer disease nest part, B is the periphery, and the hematoporphyrin derivative is made to have absorbed as a photosensitive substance beforehand in drawing 4. The 1st pulse light source that uses 31 for diagnosis, and 32 are the 2nd pulse light source used for a therapy, and are constituted from excimer die laser by each. The excimer laser which excites these two die laser is changed into the range of the number mJ - 100mJ, and oscillates the oscillation wavelength of 308 nm, 30 ns of pulse width, and energy repeatedly. The oscillation wavelength of 405 nm and the 2nd pulse light source 32 of the oscillation wavelength of the 1st pulse light source 1 is 630 nm. the change part for which 33 switches the 1st pulse light source 1 and 2nd pulse light source 32, and 34 -- as for a half mirror and 38, a television camera and 36 are [ spectrum analyzing parts and 40 ] displays for indication a spectroscopy and 39 a television monitor and 37 an optical transmission line and 35.

[0005]About diagnosis and the therapeutic device of the cancer constituted as mentioned above, the operation is explained below. First, when diagnosing cancer, the cancer disease nest part A and its periphery B are irradiated with the laser beam with a wavelength of 405 nm which made it generate according to the 1st pulse light source 31 for diagnosis via the change part 33 and the optical transmission line 34, The wavelength of 630 nm and the 690-nm fluorescence image which are excited by the laser beam with a wavelength of 405 nm are picturized with the television camera 35, and it displays on the screen of the television monitor 36, and observes. The spectrum of the fluorescence image taken out with the half mirror 37 is carried out with the spectroscopy 38, a spectrum analysis is conducted by the spectrum analyzing parts 39, and a spectrum waveform is displayed on the display for indication 40. next, when you treat cancer, the 2nd for a therapy be alike pulse light source 32 -- the cancer disease nest part A is irradiated with a laser beam with a wavelength of 630 nm made to \*\*\*\*\* via the change part 33 and the optical transmission line 34. Then, it switches to diagnosis mode again and the result of a therapy is checked. This change can be repeated and diagnosis and the therapy of cancer can be performed.

[0006]Since fluorescence peculiar to a hematoporphyrin derivative could be excited most efficiently and it was separated from its fluorescence wavelength of 630 nm, and 690 nm, the wavelength of the 1st pulse light source 31 for diagnosis was 405 nm because the influence of the scattered light was small.

The wavelength of the 2nd pulse light source 32 for a therapy was 630 nm because the laser beam of this wavelength had good tissue penetration and was efficiently absorbed by the hematoporphyrin derivative.

[0007]what was shown in (Table 1) as a photosensitive substance used for PDD and PDT besides the above conventional example is proposed -- as the laser light source respectively for PDT -- it is the same (Table 1) -- using the shown laser is examined.

[0008]

[Table 1]

光感受性物質	吸収波長〔nm〕	レーザー光源 (出射波長〔nm〕)	レーザー装置の問題点
HpD	630	エキシマダイレーザー アルゴンダイレーザー (624±8.5nm)	色素溶液の劣化が早い 大型・高価である
		金蒸気レーザー (627.8nm)	30分以上のウォームアップが必要 ガス・発振管の寿命が短い 大型・高価である
PH-1120	650	クリプトンレーザー (647nm)	ガスの寿命が短い 大型・高価である
NPe6	664	アルゴンダイレーザー (667±5nm)	色素溶液の劣化が早い 大型・高価である

[0009]

[Problem(s) to be Solved by the Invention]However, it had the problem that it was difficult to control the wavelength of the laser beam to emit by diagnosis and the therapeutic device of the above-mentioned conventional cancer.

[0010]Namely, in order to excite a photosensitive substance efficiently, It is difficult for it to be necessary to make the absorption wavelength band of a photosensitive substance agree, and to make it for wavelength of a laser beam not only to be unable to respond to the absorption wavelength band of two or more photosensitive substances of (Table 1) in a gas laser, but usually agree on the maximal absorption wavelength to one photosensitive substance. Then, as shown in the conventional example, die laser is used, but it is necessary to exchange a coloring matter solution for changing the oscillation wavelength of die laser. Therefore, when the photosensitive substance to be used is changed or the same photosensitive substance also irradiates with the laser beam of wavelength which is different in the time of diagnosis and a therapy etc., When it is necessary to change the wavelength of the laser beam with which it irradiates, it is necessary to prepare the die laser provided with several different coloring matter solutions for every required wavelength, and to switch these.

[0011]Thus, in order to prepare two or more kinds of coloring matter solutions and change parts for the case where die laser is used the 1st, it has the problem that a device is enlarged.

[0012]In the 2nd, the coloring matter solution of die laser deteriorates easily, the wavelength of

the laser beam which may be followed on this degradation changes, or an output declines. Since the stability of PDD and the laser beam with which it irradiates especially in PDT in order to make the effect into a positive thing serves as an indispensable condition, it has the problem that it is necessary to maintain exchange of a coloring matter solution, washing of a coloring matter circulation system, etc. frequently in die laser. Since wavelength changes during a laser beam exposure in the die laser which uses the early coloring matter solution of degradation or an output falls, it also has the problem that there is the necessity for detection of setting out of exposure conditions or change of a laser beam of having counted upon these change.

[0013]If die laser performs wavelength changing to the 3rd, the half breadth of the wavelength of the laser beam obtained will spread in about at least 10 nm. If the half breadth of a laser beam is wide, the energy which separates from the absorption wavelength band of a photosensitive substance will increase, and it has the problem that the excitation efficiency of a photosensitive substance worsens. Although it is possible to narrow half breadth of die laser using a bunt path filter, a diffraction grating, etc., this only cuts an excessive wavelength component and it does not become an improvement of excitation efficiency.

[0014]The excimer laser used for it as a light source which excites die laser in order to fully acquire the energy of the laser beam after wavelength changing since the energy conversion efficiency of the wavelength changing by die laser is dramatically bad to the 4th needs to be high power. Therefore, it has the problem that the diagnosis and the therapeutic device of cancer using a conventional medical-application laser device and this device are large-sized, and that it is expensive.

[0015]Since two light sources, the object for diagnosis and the object for a therapy, and the change part which switches this are needed for the 5th, while it is large-sized and expensive, it has the problem that the switching operation at the time of diagnosis and a therapy is not only inconvenient, but the danger of an operation mistake has it.

[0016]This invention solves the above-mentioned conventional problem, the miniaturization of a device is achieved, using the switch portion of a light source as unnecessary, and it aims at providing the diagnosis and the therapeutic device which also enables simultaneous diagnosis under therapy.

[0017]

[Means for Solving the Problem]To achieve the above objects, diagnosis and a therapeutic device of this invention, It diagnoses by laser beam which uses focus parts, such as cancer, for a therapy in a device diagnosed and/or treated because a photosensitive substance which has compatibility in a tumor irradiates with light from a light source a focus part made to have accumulated beforehand and excites said photosensitive substance, and a laser beam of an abbreviated identical wavelength.

[0018]



[Embodiment of the Invention] While diagnosis and the therapeutic device of this invention can make the switch portion of a light source unnecessary, can have it and being able to attain the miniaturization of a device by the above-mentioned composition, simultaneous diagnosis under therapy can also be enabled.

[0019] Hereafter, it explains, referring to drawings for the 1 embodiment of this invention.

Drawing 1 is a block diagram showing the composition of the medical-application laser device used for diagnosis and the therapeutic device of this embodiment. In drawing 1, 1 is a semiconductor laser and the temperature characteristics of  $\lambda$  and an oscillation wavelength have the characteristic that the oscillation wavelength at the time of the operation at 0 °C is 664 nm, and half breadth is [ 0.2 nm/deg and the temperature requirement which can be operated ] -100-+80 °C. The photosensitive substance 6 is prescribed for the patient and accumulated beforehand in the treated area where the optical system which branches the laser beam 3 to which 2 was emitted from the semiconductor laser 1 to the laser beam 3a for an exposure and the laser beam 3b for wavelength detection, and 4 contain an optical fiber, and 5 contains the focus part A and its periphery B. The wavelength detecting means from which 7 detects a control means, 8 detects a temperature controller, and 9 detects the wavelength of the laser beam 3b for wavelength detection, and 10 cooperate with a wavelength displaying means, 11 cooperates with the control means 7 with a shutter, and an automatic exposure inhibiting means is constituted.

[0020] The operation is explained about the medical-application laser device constituted as mentioned above. The temperature of the semiconductor laser 1 determines the wavelength of the laser beam 3 which the semiconductor laser 1 emits. That is, the wavelength of the laser beam 3 can be changed in 644-680 nm by carrying out variable control of the temperature of the semiconductor laser 1 to the range of 8-100-+80 °C of temperature controllers. Thereby, the laser beam 3 of the absorption wavelength of the photosensitive substance 6 to be used and the wavelength which suited the operating purpose can be obtained.

[0021] In this embodiment, when obtaining the laser beam 3 with a center wavelength of 664 nm of an absorption wavelength band, using NPe6 (trade name) of a chlorin system of (Table 1) as the photosensitive substance 6, temperature at 0 °C. When obtaining the laser beam 3 with the wavelength of 660 nm which is a short wavelength side in an absorption wavelength band in order to mention later, temperature was controlled at -15 °C. When obtaining the laser beam 3 which has the wavelength of 644 nm which is a short wavelength side in an absorption wavelength band about temperature at -70 °C when obtaining the laser beam 3 with a center wavelength of 650 nm of an absorption wavelength band similarly using PH-1126 (trade name) of a pheophorbide system, temperature was controlled at -100 °C.

[0022] The wavelength of the laser beam 3 which the semiconductor laser 1 emits when temperature control is carried out to said 0 °C-20 °C-70 °C and -100 °C, Since the half breadth

was  $\pm 1$  nm, the energy of the laser beam 3 suited the absorption wavelength band of the photosensitive substance 6 currently used at 663-665 nm, 659-661 nm, 649-651 nm, and 643-645 nm, respectively.

[0023] Thus, it is detected whether a part of laser beam 3 emitted from the semiconductor laser 1 which controlled temperature branches according to the optical system 2, and it is led to the wavelength detecting means 9 as the laser beam 3b for wavelength detection, and conforms to predetermined wavelength control conditions. When it is not conformed state voice, an automatic exposure inhibiting means works and a wavelength detection result intercepts the laser beam 3a for an exposure with the shutter 11, while being displayed on the wavelength displaying means 10.

[0024] When the laser beam 3 conforms to predetermined wavelength control conditions, the shutter 11 opens, and the laser beam 3a for an exposure condenses to the optical fiber 4, is irradiated, and is irradiated by the treated area 5 from the tip of the optical fiber 4.

[0025] As mentioned above, according to this embodiment, the oscillation wavelength of laser can be controlled, the absorption wavelength and the operating purpose of two or more kinds of photosensitive substances can be suited, a laser beam with wavelength with narrow half breadth can be obtained, and a photosensitive substance can be excited efficiently. A maintenance also becomes almost unnecessary and a miniaturization and low-pricing can also realize it.

[0026] Next, diagnosis and a therapeutic device are explained, referring to drawings. Drawing 2 is a block diagram showing the composition of diagnosis and the therapeutic device of the cancer in this embodiment. In drawing 2, 21 is a laser light source and is a medical-application laser device using the semiconductor laser explained above. The optical transmission line where 22 draws the laser beam 3a for an exposure from the laser light source 21 near a focus part, and 23 are the picture transmission ways by the fluorescence for observing a focus part and its circumference, and 24 is a light guide machine which contains the optical transmission line 22 and the picture transmission way 23, and is led near a focus part. 25 picturizes and carries out analysis processing of the picture near [ which is image pick-up / analysis means, and is obtained through the picture transmission way 23 ] a focus part, and this result is displayed on the image display means 26. 27 is band pass filters (for example, all the dielectric interference filter DIF type etc. of Optical Coatings Japan, Inc. with the characteristic shown in drawing 3) with a very narrow bandwidth of about  $\pm 3$  nm to the specification wavelength which comprised a dielectric multilayer, It is what can penetrate only the light near the fluorescence wavelength (it is about 654 nm at the time of about 670 nm and a pheophorbide system photosensitive substance in the case of a chlorin system photosensitive substance) of the photosensitive substance to be used in distinction from the wavelength of the laser beam 3a for an exposure, It is arranged on the optical path which connects image pick-up / analysis

means 25 to the picture transmission way 23. The band pass filter 27 is provided with the switching means (not shown) of owner *Perilla frutescens* (L.) Britton var. *crispa* (Thunb.) Decne. for two or more kinds of band pass filters which are adapted for two or more kinds of photosensitive substances, respectively. Numerals, such as the treated area 5 of drawing 2, are the same as that of drawing 1.

[0027]The operation is explained about diagnosis and the therapeutic device of the cancer constituted as mentioned above. First, the laser beam 3a for an exposure emitted from the laser light source 21 is irradiated via the optical transmission line 22 by the treated area 5 on which the photosensitive substance was made to accumulate beforehand. At this time, the wavelength of the laser beam 3a for an exposure is controlled using a temperature controller to become a center wavelength of the absorption wavelength band of the photosensitive substance which becomes the optimal [ a curative effect ] corresponding to the photosensitive substance currently used. That is, when a photosensitive substance is NPe6 of a chlorin system, in the case of PH-1126 of 664 nm and a pheophorbide system, it controls to 650 nm. Operation of this wavelength control was already described.

[0028]And if the laser beam 3a for an exposure is irradiated by the treated area 5, while the focus part A will be selectively treated by operation of the photosensitive substance made to accumulate beforehand, a fluorescence of the specific wavelength which the photosensitive substance of the focus part A was excited and was mentioned above is shown. Although the treated area 5 is diagnosed by picturizing and analyzing the picture by this fluorescence, the wavelength of this fluorescence is approximated with the wavelength of the laser beam 3a for an exposure, and also since intensity is weak, generally an image pick-up and analysis of a receptacle picture are strongly difficult in the influence of the scattered light of the laser beam 3a for an exposure.

[0029]However, after drawing this fluorescence on the picture transmission way 23, it has the characteristic as showed drawing 3 one of them, By letting the band pass filter 27 which penetrates only the wavelength of the fluorescence which the photosensitive substance currently used shows, and intercepts the wavelength of the laser beam 3a for an exposure pass, the influence of the scattered light of the laser beam 3a for an exposure is eliminated, and only a fluorescent image is inputted into image pick-up / analysis means 25. Image pick-up / analysis means 25 picturizes and carries out analysis processing of the picture information by this fluorescence, and that analysis result is displayed on the image display means 26. The focus part A can be diagnosed in real time also during a therapy by observing this display.

[0030]Control which shifts the wavelength of the laser beam 3a for an exposure in the direction separated from the wavelength of fluorescence in order to improve more separation (S/N ratio) of the scattered light (N) of fluorescence (S) and the laser beam 3a for an exposure can also be performed. Namely, the center wavelength of the absorption wavelength band of the

photosensitive substance which is using the wavelength of the laser beam 3a for an exposure. (for example, in the case of NPe6, in the case of 664 nm and PH-1126, it keeps away from a fluorescence wavelength in the range of 650-nm) to an absorption wavelength band -- as (they are 660 nm and 644 nm in the case of PH-1126 in the case of for example, NPe6) -- wavelength control is carried out so that it may shift. If it controls in this way, the S/N ratio of the scattered light of fluorescence and the laser beam 3a for an exposure will be improved, it is Example 1 simultaneously, as already explained, the energy of the laser beam 3a for an exposure is in the absorption wavelength band of the photosensitive substance currently used, and there is almost no fall of a curative effect.

[0031]Even if it is in the diagnosis and the therapeutic device which uses only a specific photosensitive substance in order to realize what was described here (for example, NPe6, PH-1126, etc.), it is the range of the effective absorption wavelength of the photosensitive substance (for example, in the case of NPe6 of a chlorin system, 664\*\*5 nm) about the oscillation wavelength of the laser beam 3. In the case of PH-1126 of a pheophorbide system, it was made into 650\*\*10 nm etc. with variable.

[0032]Since the medical-application laser device in this embodiment can control easily the wavelength of the laser beam 3a for an exposure, when the simultaneous diagnosis under therapy becomes unnecessary, the wavelength of the laser beam 3a for an exposure can also be returned to the center wavelength of the absorption wavelength band of the optimal photosensitive substance for a therapy. When it indicated whether the medical-application laser device in this embodiment suited the wave number or wavelength control conditions of the laser beam 3 which are emitted or the wavelength of the laser beam 3 did not conform to wavelength control conditions, the laser beam also already said that it does not glare.

[0033]As mentioned above, according to this embodiment, the wavelength of the fluorescence which a photosensitive substance shows by a laser beam is penetrated, and therapy and diagnosis can be performed in a single laser light source by having a band pass filter which intercepts the wavelength of a laser beam. When a wavelength control means shifts the wavelength of a laser beam so that it may keep away from the fluorescence wavelength which this photosensitive substance emits in the absorption wavelength band of a photosensitive substance, the S/N ratio where the picture was stabilized also in the simultaneous diagnosis under therapy is securable.

[0034]In the above-mentioned explanation, although laser was used as the semiconductor laser, the half breadth of laser of a laser beam is narrow, and its oscillation wavelength of a laser beam is good also as other laser which is variable. It cannot be overemphasized that the semiconductor 1 is not what is limited to what has the characteristic raised to the above-mentioned embodiment.

[0035]Although this embodiment showed again the example which performs feedback control

using the wavelength detecting means 9 as temperature control, Exact wavelength control is possible also by having the memory measure which memorized beforehand the temperature of a semiconductor laser and the relation of an oscillation wavelength to be used, and controlling the temperature of a semiconductor based on this relation.

[0036]

[Effect of the Invention]Diagnosis and the therapeutic device of this invention can make the switch portion of a light source unnecessary, and it can also enable simultaneous diagnosis under therapy while it can have it and it can attain the miniaturization of a device, so that clearly from the above explanation.

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**TECHNICAL FIELD**

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[Field of the Invention]The photosensitive substance which has compatibility in a tumor irradiates with the light corresponding to the absorption wavelength of the photosensitive substance the focus part of tumors, such as cancer made to have accumulated beforehand, and this invention excites a photosensitive substance, and relates to the diagnosis and the therapeutic device which diagnoses and/or treats a focus part.

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**PRIOR ART**

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[Description of the Prior Art]In recent years, the photochemistry diagnosis (it is described as Photodynamic Diagnosis and following PDD) and the photochemistry therapy (it is described as PhotodynamicTherapy and the following PDT) using a laser beam are developing quickly with progress of the electronic iatrotechnique. The photosensitive substance which has photochemical reactions, such as firefly luminescence and a cytocidal action, when it has compatibility in a tumor and is excited by light in this PDD and PDT is made to accumulate on the focus part of tumors, such as cancer, beforehand, By irradiating this focus part, a photosensitive substance is excited and the diagnosis (PDD) of a focus part by measurement of that luminescence fluorescence and the focus part by cytotoxicity reaction are treated (PDT). Since it is better for the wavelength of irradiation light to have agreed in the absorption wavelength of a photosensitive substance in order to excite a photosensitive substance efficiently, the laser light source of the wavelength which suited the absorption wavelength of the photosensitive substance used as a light source of irradiation light is used.

[0003]As diagnosis and a therapeutic device of this kind of cancer, conventionally, . Were indicated by JP,63-2633,B and JP,63-9464,B. The device using the die laser (henceforth excimer die laser) excited using excimer laser as a laser light source is known well, using a hematoporphyrin derivative as a photosensitive substance. It explains referring to drawings for the diagnosis and the therapeutic device of cancer using the conventional laser device indicated by JP,63-2633,B and JP,63-9464,B hereafter.

[0004]Drawing 4 shows the outline lineblock diagram of the diagnosis and the therapeutic device of cancer using the conventional laser device. A is a cancer disease nest part, B is the periphery, and the hematoporphyrin derivative is made to have absorbed as a photosensitive substance beforehand in drawing 4. The 1st pulse light source that uses 31 for diagnosis, and 32 are the 2nd pulse light source used for a therapy, and are constituted from excimer die laser by each. The excimer laser which excites these two die laser is changed into the range of

the number mJ - 100mJ, and oscillates the oscillation wavelength of 308 nm, 30 ns of pulse width, and energy repeatedly. The oscillation wavelength of 405 nm and the 2nd pulse light source 32 of the oscillation wavelength of the 1st pulse light source 1 is 630 nm. the change part for which 33 switches the 1st pulse light source 1 and 2nd pulse light source 32, and 34 -- as for a half mirror and 38, a television camera and 36 are [ spectrum analyzing parts and 40 ] displays for indication a spectroscopy and 39 a television monitor and 37 an optical transmission line and 35.

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[0006]Since fluorescence peculiar to a hematoporphyrin derivative could be excited most efficiently and it was separated from its fluorescence wavelength of 630 nm, and 690 nm, the wavelength of the 1st pulse light source 31 for diagnosis was 405 nm because the influence of the scattered light was small.

The wavelength of the 2nd pulse light source 32 for a therapy was 630 nm because the laser beam of this wavelength had good tissue penetration and was efficiently absorbed by the hematoporphyrin derivative.

[0007]what was shown in (Table 1) as a photosensitive substance used for PDD and PDT besides the above conventional example is proposed -- as the laser light source respectively for PDT -- it is the same (Table 1) -- using the shown laser is examined.

[0008]

[Table 1]



光感受性 物質	吸収波長 (nm)	レーザー光源 (出射波長 (nm))	レーザー装置の問題点
HpD	630	エキシマダイレーザー アルゴンダイレーザー (624 ± 6.5 nm)	色素溶液の劣化が早い 大型・高価である
		金蒸気レーザー (627.8 nm)	30分以上のウォームアップが 必要 ガス・発振管の寿命が短い 大型・高価である
PH- 1126	650	クリプトンレーザー (647 nm)	ガスの寿命が短い 大型・高価である
NPe8	664	アルゴンダイレーザー (667 ± 5 nm)	色素溶液の劣化が早い 大型・高価である

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**EFFECT OF THE INVENTION**

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[Effect of the Invention]Diagnosis and the therapeutic device of this invention can make the switch portion of a light source unnecessary, and it can also enable simultaneous diagnosis under therapy while it can have it and it can attain the miniaturization of a device, so that clearly from the above explanation.

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**TECHNICAL PROBLEM**

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[Problem(s) to be Solved by the Invention]However, it had the problem that it was difficult to control the wavelength of the laser beam to emit by diagnosis and the therapeutic device of the above-mentioned conventional cancer.

[0010]Namely, in order to excite a photosensitive substance efficiently, It is difficult for it to be necessary to make the absorption wavelength band of a photosensitive substance agree, and to make it for wavelength of a laser beam not only to be unable to to respond to the absorption wavelength band of two or more photosensitive substances of (Table 1) in a gas laser, but usually agree on the maximal absorption wavelength to one photosensitive substance. Then, as shown in the conventional example, die laser is used, but it is necessary to exchange a coloring matter solution for changing the oscillation wavelength of die laser. Therefore, when the photosensitive substance to be used is changed or the same photosensitive substance also irradiates with the laser beam of wavelength which is different in the time of diagnosis and a therapy etc., When it is necessary to change the wavelength of the laser beam with which it irradiates, it is necessary to prepare the die laser provided with several different coloring matter solutions for every required wavelength, and to switch these.

[0011]Thus, in order to prepare two or more kinds of coloring matter solutions and change parts for the case where die laser is used the 1st, it has the problem that a device is enlarged.  
[0012]In the 2nd, the coloring matter solution of die laser deteriorates easily, the wavelength of the laser beam which may be followed on this degradation changes, or an output declines. Since the stability of PDD and the laser beam with which it irradiates especially in PDT in order to make the effect into a positive thing serves as an indispensable condition, it has the problem that it is necessary to maintain exchange of a coloring matter solution, washing of a coloring matter circulation system, etc. frequently in die laser. Since wavelength changes during a laser beam exposure in the die laser which uses the early coloring matter solution of degradation or an output falls, it also has the problem that there is the necessity for detection of setting out of

exposure conditions or change of a laser beam of having counted upon these change.

[0013]If die laser performs wavelength changing to the 3rd, the half breadth of the wavelength of the laser beam obtained will spread in about at least 10 nm. If the half breadth of a laser beam is wide, the energy which separates from the absorption wavelength band of a photosensitive substance will increase, and it has the problem that the excitation efficiency of a photosensitive substance worsens. Although it is possible to narrow half breadth of die laser using a bunt path filter, a diffraction grating, etc., this only cuts an excessive wavelength component and it does not become an improvement of excitation efficiency.

[0014]The excimer laser used for it as a light source which excites die laser in order to fully acquire the energy of the laser beam after wavelength changing since the energy conversion efficiency of the wavelength changing by die laser is dramatically bad to the 4th needs to be high power. Therefore, it has the problem that the diagnosis and the therapeutic device of cancer using a conventional medical-application laser device and this device are large-sized, and that it is expensive.

[0015]Since two light sources, the object for diagnosis and the object for a therapy, and the change part which switches this are needed for the 5th, while it is large-sized and expensive, it has the problem that the switching operation at the time of diagnosis and a therapy is not only inconvenient, but the danger of an operation mistake has it.

[0016]This invention solves the above-mentioned conventional problem, the miniaturization of a device is achieved, using the switch portion of a light source as unnecessary, and it aims at providing the diagnosis and the therapeutic device which also enables simultaneous diagnosis under therapy.

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[Translation done.]

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## MEANS

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[Means for Solving the Problem]To achieve the above objects, diagnosis and a therapeutic device of this invention, It diagnoses by laser beam which uses focus parts, such as cancer, for a therapy in a device diagnosed and/or treated because a photosensitive substance which has compatibility in a tumor irradiates with light from a light source a focus part made to have accumulated beforehand and excites said photosensitive substance, and a laser beam of an abbreviated identical wavelength.

[0018]

[Embodiment of the Invention]While diagnosis and the therapeutic device of this invention can make the switch portion of a light source unnecessary, can have it and being able to attain the miniaturization of a device by the above-mentioned composition, simultaneous diagnosis under therapy can also be enabled.

[0019]Hereafter, it explains, referring to drawings for the 1 embodiment of this invention.

Drawing 1 is a block diagram showing the composition of the medical-application laser device used for diagnosis and the therapeutic device of this embodiment. In drawing 1, 1 is a semiconductor laser and the temperature characteristics of \*\*1 nm and an oscillation wavelength have the characteristic that the oscillation wavelength at the time of the operation at 0 \*\* is 664 nm, and half breadth is [ 0.2 nm/deg and the temperature requirement which can be operated ] -100-+80 \*\*. The photosensitive substance 6 is prescribed for the patient and accumulated beforehand in the treated area where the optical system which branches the laser beam 3 to which 2 was emitted from the semiconductor laser 1 to the laser beam 3a for an exposure and the laser beam 3b for wavelength detection, and 4 contain an optical fiber, and 5 contains the focus part A and its periphery B. The wavelength detecting means from which 7 detects a control means, 8 detects a temperature controller, and 9 detects the wavelength of the laser beam 3b for wavelength detection, and 10 cooperate with a wavelength displaying means, 11 cooperates with the control means 7 with a shutter, and an

automatic exposure inhibiting means is constituted.

[0020]The operation is explained about the medical-application laser device constituted as mentioned above. The temperature of the semiconductor laser 1 determines the wavelength of the laser beam 3 which the semiconductor laser 1 emits. That is, the wavelength of the laser beam 3 can be changed in 644-680 nm by carrying out variable control of the temperature of the semiconductor laser 1 to the range of 8-100-+80 ° of temperature controllers. Thereby, the laser beam 3 of the absorption wavelength of the photosensitive substance 6 to be used and the wavelength which suited the operating purpose can be obtained.

[0021]In this embodiment, when obtaining the laser beam 3 with a center wavelength of 664 nm of an absorption wavelength band, using NPe6 (trade name) of a chlorin system of (Table 1) as the photosensitive substance 6, temperature at 0 °. When obtaining the laser beam 3 with the wavelength of 660 nm which is a short wavelength side in an absorption wavelength band in order to mention later, temperature was controlled at -15 °. When obtaining the laser beam 3 which has the wavelength of 644 nm which is a short wavelength side in an absorption wavelength band about temperature at -70 ° when obtaining the laser beam 3 with a center wavelength of 650 nm of an absorption wavelength band similarly using PH-1126 (trade name) of a pheophorbide system, temperature was controlled at -100 °.

[0022]The wavelength of the laser beam 3 which the semiconductor laser 1 emits when temperature control is carried out to said 0 °-20 °-70 ° and -100 °, Since the half breadth was 1 nm, the energy of the laser beam 3 suited the absorption wavelength band of the photosensitive substance 6 currently used at 663-665 nm, 659-661 nm, 649-651 nm, and 643-645 nm, respectively.

[0023]Thus, it is detected whether a part of laser beam 3 emitted from the semiconductor laser 1 which controlled temperature branches according to the optical system 2, and it is led to the wavelength detecting means 9 as the laser beam 3b for wavelength detection, and conforms to predetermined wavelength control conditions. When it is not conformed state voice, an automatic exposure inhibiting means works and a wavelength detection result intercepts the laser beam 3a for an exposure with the shutter 11, while being displayed on the wavelength displaying means 10.

[0024]When the laser beam 3 conforms to predetermined wavelength control conditions, the shutter 11 opens, and the laser beam 3a for an exposure condenses to the optical fiber 4, is irradiated, and is irradiated by the treated area 5 from the tip of the optical fiber 4.

[0025]As mentioned above, according to this embodiment, the oscillation wavelength of laser can be controlled, the absorption wavelength and the operating purpose of two or more kinds of photosensitive substances can be suited, a laser beam with wavelength with narrow half breadth can be obtained, and a photosensitive substance can be excited efficiently. A maintenance also becomes almost unnecessary and a miniaturization and low-pricing can also

realize it.

[0026]Next, diagnosis and a therapeutic device are explained, referring to drawings. Drawing 2 is a block diagram showing the composition of diagnosis and the therapeutic device of the cancer in this embodiment. In drawing 2, 21 is a laser light source and is a medical-application laser device using the semiconductor laser explained above. The optical transmission line where 22 draws the laser beam 3a for an exposure from the laser light source 21 near a focus part, and 23 are the picture transmission ways by the fluorescence for observing a focus part and its circumference, and 24 is a light guide machine which contains the optical transmission line 22 and the picture transmission way 23, and is led near a focus part. 25 picturizes and carries out analysis processing of the picture near [ which is image pick-up / analysis means, and is obtained through the picture transmission way 23 ] a focus part, and this result is displayed on the image display means 26. 27 is band pass filters (for example, all the dielectric interference filter DIF type etc. of Optical Coatings Japan, Inc. with the characteristic shown in drawing 3) with a very narrow bandwidth of about  $\pm 3$  nm to the specification wavelength which comprised a dielectric multilayer, It is what can penetrate only the light near the fluorescence wavelength (it is about 654 nm at the time of about 670 nm and a pheophorbide system photosensitive substance in the case of a chlorin system photosensitive substance) of the photosensitive substance to be used in distinction from the wavelength of the laser beam 3a for an exposure, It is arranged on the optical path which connects image pick-up / analysis means 25 to the picture transmission way 23. The band pass filter 27 is provided with the switching means (not shown) of owner *Perilla frutescens* (L.) Britton var. *crispa* (Thunb.) Decne. for two or more kinds of band pass filters which are adapted for two or more kinds of photosensitive substances, respectively. Numerals, such as the treated area 5 of drawing 2, are the same as that of drawing 1.

[0027]The operation is explained about diagnosis and the therapeutic device of the cancer constituted as mentioned above. First, the laser beam 3a for an exposure emitted from the laser light source 21 is irradiated via the optical transmission line 22 by the treated area 5 on which the photosensitive substance was made to accumulate beforehand. At this time, the wavelength of the laser beam 3a for an exposure is controlled using a temperature controller to become a center wavelength of the absorption wavelength band of the photosensitive substance which becomes the optimal [ a curative effect ] corresponding to the photosensitive substance currently used. That is, when a photosensitive substance is NP6 of a chlorin system, in the case of PH-1126 of 664 nm and a pheophorbide system, it controls to 650 nm. Operation of this wavelength control was already described.

[0028]And if the laser beam 3a for an exposure is irradiated by the treated area 5, while the focus part A will be selectively treated by operation of the photosensitive substance made to accumulate beforehand, a fluorescence of the specific wavelength which the photosensitive

substance of the focus part A was excited and was mentioned above is shown. Although the treated area 5 is diagnosed by picturizing and analyzing the picture by this fluorescence, the wavelength of this fluorescence is approximated with the wavelength of the laser beam 3a for an exposure, and also since intensity is weak, generally an image pick-up and analysis of a receptacle picture are strongly difficult in the influence of the scattered light of the laser beam 3a for an exposure.

[0029]However, after drawing this fluorescence on the picture transmission way 23, it has the characteristic as showed drawing 3 one of them, By letting the band pass filter 27 which penetrates only the wavelength of the fluorescence which the photosensitive substance currently used shows, and intercepts the wavelength of the laser beam 3a for an exposure pass, the influence of the scattered light of the laser beam 3a for an exposure is eliminated, and only a fluorescent image is inputted into image pick-up / analysis means 25. Image pick-up / analysis means 25 picturizes and carries out analysis processing of the picture information by this fluorescence, and that analysis result is displayed on the image display means 26. The focus part A can be diagnosed in real time also during a therapy by observing this display.

[0030]Control which shifts the wavelength of the laser beam 3a for an exposure in the direction separated from the wavelength of fluorescence in order to improve more separation (S/N ratio) of the scattered light (N) of fluorescence (S) and the laser beam 3a for an exposure can also be performed. Namely, the center wavelength of the absorption wavelength band of the photosensitive substance which is using the wavelength of the laser beam 3a for an exposure. (for example, in the case of NPe6, in the case of 664 nm and PH-1126, it keeps away from a fluorescence wavelength in the range of 650-nm) to an absorption wavelength band -- as (they are 660 nm and 644 nm in the case of PH-1126 in the case of for example, NPe6) -- wavelength control is carried out so that it may shift. If it controls in this way, the S/N ratio of the scattered light of fluorescence and the laser beam 3a for an exposure will be improved, it is Example 1 simultaneously, as already explained, the energy of the laser beam 3a for an exposure is in the absorption wavelength band of the photosensitive substance currently used, and there is almost no fall of a curative effect.

[0031]Even if it is in the diagnosis and the therapeutic device which uses only a specific photosensitive substance in order to realize what was described here (for example, NPe6, PH-1126, etc.), it is the range of the effective absorption wavelength of the photosensitive substance (for example, in the case of NPe6 of a chlorin system, 664\*\*5 nm) about the oscillation wavelength of the laser beam 3. In the case of PH-1126 of a pheophorbide system, it was made into 650\*\*10 nm etc. with variable.

[0032]Since the medical-application laser device in this embodiment can control easily the wavelength of the laser beam 3a for an exposure, when the simultaneous diagnosis under therapy becomes unnecessary, the wavelength of the laser beam 3a for an exposure can also



be returned to the center wavelength of the absorption wavelength band of the optimal photosensitive substance for a therapy. When it indicated whether the medical-application laser device in this embodiment suited the wave number or wavelength control conditions of the laser beam 3 which are emitted or the wavelength of the laser beam 3 did not conform to wavelength control conditions, the laser beam also already said that it does not glare.

[0033]As mentioned above, according to this embodiment, the wavelength of the fluorescence which a photosensitive substance shows by a laser beam is penetrated, and therapy and diagnosis can be performed in a single laser light source by having a band pass filter which intercepts the wavelength of a laser beam. When a wavelength control means shifts the wavelength of a laser beam so that it may keep away from the fluorescence wavelength which this photosensitive substance emits in the absorption wavelength band of a photosensitive substance, the S/N ratio where the picture was stabilized also in the simultaneous diagnosis under therapy is securable.

[0034]In the above-mentioned explanation, although laser was used as the semiconductor laser, the half breadth of laser of a laser beam is narrow, and its oscillation wavelength of a laser beam is good also as other laser which is variable. It cannot be overemphasized that the semiconductor 1 is not what is limited to what has the characteristic raised to the above-mentioned embodiment.

[0035]Although this embodiment showed again the example which performs feedback control using the wavelength detecting means 9 as temperature control, Exact wavelength control is possible also by having the memory measure which memorized beforehand the temperature of a semiconductor laser and the relation of an oscillation wavelength to be used, and controlling the temperature of a semiconductor based on this relation.

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**DESCRIPTION OF DRAWINGS**

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[Brief Description of the Drawings]

[Drawing 1]The block diagram showing the composition of the medical-application laser device in the 1 embodiment of this invention

[Drawing 2]The block diagram showing the composition of the diagnosis and the therapeutic device in the 1 embodiment of this invention

[Drawing 3]The characteristic figure of the band pass filter used with the said diagnosis and a therapeutic device

[Drawing 4]The block diagram showing the composition of the diagnosis and the therapeutic device of cancer using the conventional laser device

[Description of Notations]

1 Semiconductor laser (laser)

3 Laser beam

5 Treated area (focus part)

6 Photosensitive substance

8 Temperature controller (wavelength control means)

21 Laser light source (medical-application laser device)

22 Optical transmission line

23 Picture transmission way

25 Image pick-up / analysis means

26 Image display means

27 Band pass filter (fluorescence separating mechanism)

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[Translation done.]

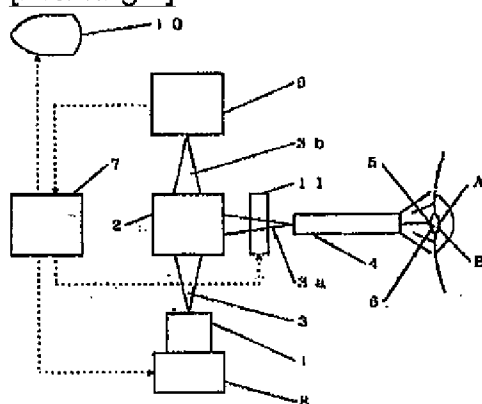
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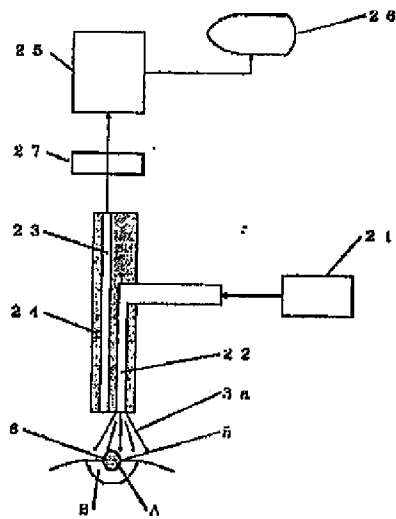
## DRAWINGS

[Drawing 1]



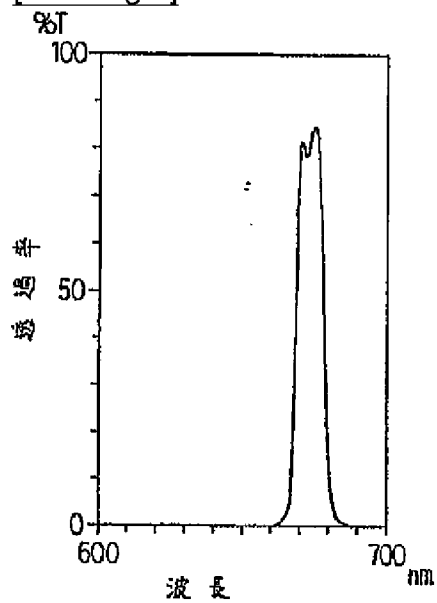
- 1 半導体レーザー (レーザー)
- 3 レーザ光
- 5 治療部位
- 6 光感受性物質
- 8 温度制御装置 (温度制御手段)

[Drawing 2]

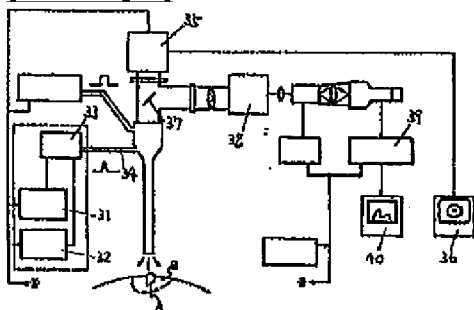


- 21 レーザ光源 (固有用レーザー装置)  
 22 光伝送路  
 23 画像伝送路  
 25 撮像・解析手段  
 26 画像表示手段  
 27 バンドパスフィルタ (分光分離手段)

[Drawing 3]



[Drawing 4]



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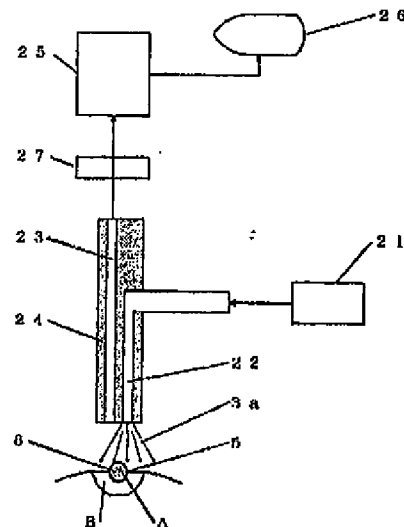
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(54) 【発明の名称】 診断・治療装置

(57) 【要約】

【課題】 光化学診断および光化学治療に用いる光源として複数種類の光感受性物質や励起条件に合った発振波長のレーザー光が得られる医療用レーザー装置を用いて単一光源で診断と治療を可能とし、治療中の同時診断をも可能とする診断・治療装置を提供する。

【解決手段】 光源としてレーザー光の半値幅が狭くレーザー光の発振波長を可変とした半導体レーザーを用いた医療用レーザー装置21と、前記医療用レーザー装置21が射出する照射用レーザー光3aを病巣部5付近に導くための光伝送路22と、病巣部5およびその周辺を観察するための画像伝送路23と、照射用レーザー光3aにより光感受性物質が発する蛍光のみを分離する蛍光分離手段27と、前記蛍光分離手段により得られた蛍光像を撮像し解析処理する撮像・解析手段25と、前記解析処理結果を表示する画像表示手段26とを備える。



- 21 レーザ光源 (医療用レーザー装置)
- 22 光伝送路
- 23 画像伝送路
- 25 撮像・解析手段
- 26 画像表示手段
- 27 バンドパスフィルタ (蛍光分離手段)

## 【特許請求の範囲】

【請求項1】腫瘍に親和性のある光感受性物質があらかじめ集積させてある病巣部に光源からの光を照射して前記光感受性物質を励起することで、癌などの病巣部を診断および／または治療する装置において、治療に用いるレーザ光と略同一波長のレーザ光で診断を行う診断・治療装置。

【請求項2】治療と診断を同時に行う請求項1記載の診断・治療装置。

【請求項3】治療に用いるレーザ光の波長および診断に用いるレーザ光の波長のいずれもが光感受性物質の吸収波長帯内にある請求項1または2記載の診断・治療装置。

【請求項4】治療用のレーザ光と診断用のレーザ光とを照射するために単一のレーザ光源を備えた請求項1または2または3記載の診断・治療装置。

【請求項5】治療用のレーザ光と診断用のレーザ光の半値幅が光感受性物質の吸収波長帯の内治療時に選択する吸収波長帯の幅よりも狭いととも、前記治療用のレーザ光および前記診断用のレーザ光と、前記光感受性物質が発する蛍光とを分離する蛍光分離手段を備えた請求項1または2または3記載の診断・治療装置。

【請求項6】レーザ光を病巣部付近に導く光伝送路と、前記レーザ光により励起された光感受性物質が発する蛍光を導く画像伝送路と、前記蛍光のみを分離する蛍光分離手段と、前記蛍光分離手段により得られた蛍光像を撮像し解析処理する撮像・解析手段と、前記蛍光像の解析処理結果を表示する画像表示手段とを備え、前記蛍光像を前記病巣部の治療中にも前記画像表示手段で表示する請求項2または3記載の診断・治療装置。

## 【発明の詳細な説明】

## 【0001】

【発明の属する技術分野】本発明は腫瘍に親和性のある光感受性物質があらかじめ集積させてある癌など腫瘍の病巣部に、光感受性物質の吸収波長に合致した光を照射して光感受性物質を励起し、病巣部を診断および／または治療する診断・治療装置に関する。

## 【0002】

【従来の技術】近年、電子医療技術の進歩にともなう、レーザ光を用いた光化学診断(Photodynamic Diagnosis、以下PDDと記す)および光化学治療(Photodynamic Therapy、以下PDTと記す)が急速に発展しつつある。このPDDおよびPDTとは、腫瘍に親和性を有し、かつ光により励起されたときに蛍光発光や殺細胞作用などの光化学反応を有する光感受性物質をあらかじめ癌など腫瘍の病巣部に集積させておき、この病巣部に光を照射することにより光感受性物質を励起して、その発光蛍光の測定による病巣部の診断(PDD)や、殺細胞効果による病巣部の治療(PDT)を行なうものである。光感受性物質を効率良く励起するには、照射光の波

長が光感受性物質の吸収波長に合致している方が良いので、照射光の光源としては使用する光感受性物質の吸収波長に適合した波長のレーザ光源が使用される。

【0003】従来、この種の癌の診断・治療装置としては、特公昭63-2633号公報および特公昭63-9464号公報によって開示された、光感受性物質としてヘマトポルフィリン誘導体を用い、レーザ光源としてエキシマレーザを用いて励起されるダイレーザ(以下エキシマ・ダイレーザという)を用いる装置がよく知られている。以下、特公昭63-2633号公報および特公昭63-9464号公報によって開示された従来のレーザ装置を用いた癌の診断・治療装置について図面を参照しながら説明する。

【0004】図4は従来のレーザ装置を用いた癌の診断・治療装置の概略構成図を示すものである。図4において、Aは癌病巣部、Bはその周辺部で、あらかじめ光感受性物質としてヘマトポルフィリン誘導体を吸収させてある。31は診断に用いる第1のパルス光源、32は治療に用いる第2のパルス光源で、いずれもエキシマ・ダイレーザで構成されている。この2つのダイレーザを励起するエキシマレーザは発振波長308nm、パルス幅30ns、エネルギーは数mJ~100mJの範囲に可変して繰り返し発振する。第1のパルス光源1の発振波長は405nm、第2のパルス光源32の発振波長は630nmである。33は第1のパルス光源1と第2のパルス光源32とを切換える切換え部、34は光伝送路、35はテレビカメラ、36はテレビモニタ、37はハーフミラー、38は分光器、39はスペクトラム解析部、40は表示器である。

【0005】以上のように構成された癌の診断・治療装置について、以下その動作を説明する。まず、癌の診断を行うときは、診断用の第1のパルス光源31によって発生させた波長405nmのレーザ光を切換え部33および光伝送路34を介して癌病巣部Aおよびその周辺部Bに照射し、波長405nmのレーザ光によって励起される波長630nmおよび690nmの蛍光像をテレビカメラ35によって撮像し、テレビモニタ36の画面上に表示して観察する。また、ハーフミラー37によって取り出された蛍光像を分光器38で分光し、スペクトラム解析部39でスペクトル分析して表示器40にスペクトラム波形を表示する。つぎに、癌の治療を行うときは、治療用の第2のパルス光源32によって発生させた波長630nmのレーザ光を切換え部33および光伝送路34を介して癌病巣部Aに照射する。その後、ふたたび診断モードに切換えて治療の結果を確認する。この切換えを繰り返して癌の診断・治療を行うことができる。

【0006】診断用の第1のパルス光源31の波長を405nmとしたのは、ヘマトポルフィリン誘導体特有の蛍光を最も効率よく励起することができ、その蛍光波長630nmおよび690nmとは離れているので散乱光

の影響が小さいためであり、治療用の第2のバルス光源32の波長を630nmにしたのは、この波長のレーザー光が組織透過性が高く、ヘマトポルフィリン誘導体に効率よく吸収されるからである。

【0007】以上の従来例のほか、PDDおよびPDTに用いられる光感受性物質として例えば(表1)に示し

光感受性物質	吸収波長[nm]	レーザー光源(出射波長[nm])	レーザー装置の問題点
HpD	630	エキシマダイレーザー アルゴンダイレーザー (624±8.5nm)	色素溶液の劣化が早い 大型・高価である
		金蒸気レーザー (627.8nm)	30分以上のウォームアップが必要 ガス・発振管の寿命が短い 大型・高価である
PH-1126	660	クリプトンレーザー (647nm)	ガスの寿命が短い 大型・高価である
NPe6	664	アルゴンダイレーザー (667±5nm)	色素溶液の劣化が早い 大型・高価である

【0009】

【発明が解決しようとする課題】しかしながら上記従来の癌の診断・治療装置では、出射するレーザー光の波長を制御することが困難であるという問題点を有していた。

【0010】すなわち、光感受性物質を効率良く励起するには、レーザー光の波長を光感受性物質の吸収波長帯に合致させる必要があり、通常、ガスレーザーでは(表1)の複数の光感受性物質の吸収波長帯に対応することができないばかりでなく、一つの光感受性物質に対しても、その最大吸収波長に合致させることは困難である。そこで、従来例に示したようにダイレーザーが使用されるが、ダイレーザーの発振波長を変えるには色素溶液を交換する必要がある。そのため、使用する光感受性物質を変えたり、同じ光感受性物質でも診断時と治療時で異なる波長のレーザー光を照射する場合など、照射するレーザー光の波長を変える必要があるときには、必要な波長ごとに異なる複数の色素溶液を備えたダイレーザーを用意し、これらを切換える必要がある。

【0011】このように、ダイレーザーを用いる場合には、第1に複数種類の色素溶液と、その切換え部を備えるため装置が大型化するという問題点を有している。

【0012】第2に、ダイレーザーの色素溶液は劣化しやすく、この劣化に伴い得られるレーザー光の波長が変化したり出力が低下したりする。PDDや、とくにPDTにおいては、その効果を確実なものにするためには照射するレーザー光の安定性が必須条件となるので、ダイレーザーにおいては色素溶液の交換や色素循環装置の洗浄などのメンテナンスを頻繁に行う必要があるという問題点を有している。また、劣化の早い色素溶液を使用したダイ

タものが提案され、それぞれPDT用のレーザー光源として同じく(表1)に示したレーザーを用いることが検討されている。

【0008】

【表1】

レーザーにおいてはレーザー光照射中に波長が変化したり出力が落ちたりすることもあり、これらの変化を見込んだ照射条件の設定やレーザー光の変化の検出の必要があるという問題点も有している。

【0013】第3に、ダイレーザーによって波長変換を行なうと、得られるレーザー光の波長の半値幅は少なくとも10nm程度に広がってしまう。レーザー光の半値幅が広いと光感受性物質の吸収波長帯をはずれるエネルギーが増え、光感受性物質の励起効率が悪くなるという問題点を有している。なお、バンドパスフィルターや回折格子などを用いてダイレーザーの半値幅を狭くすることは可能であるが、これは余分な波長成分をカットするだけであり、励起効率の改善にはならない。

【0014】第4に、ダイレーザーによる波長変換のエネルギー変換効率は非常に悪いので、波長変換後のレーザー光のエネルギーを十分に得るためにはダイレーザーを励起する光源として用いられるエキシマレーザーなどは高出力である必要がある。そのため、従来の医療用レーザー装置およびこの装置を用いた癌の診断・治療装置は大型・高価であるという問題点を有している。

【0015】第5に、診断用と治療用の二つの光源とこれを切換える切換え部を必要とするため、大型・高価であるとともに、診断・治療時の切換え操作が不便であるばかりでなく誤操作の危険もあるという問題点を有している。

【0016】本発明は上記従来の問題点を解決するもので、光源の切り換え部を不要として装置の小型化をはかり、治療中の同時診断をも可能とする診断・治療装置を提供することを目的とする。



## 【0017】

【課題を解決するための手段】上記目的を達成するために本発明の診断・治療装置は、腫瘍に親和性のある光感受性物質があらかじめ集積させてある病巣部に光源からの光を照射して前記光感受性物質を励起することで、癌などの病巣部を診断および／または治療する装置において、治療に用いるレーザー光と略同一波長のレーザー光で診断を行うものである。

## 【0018】

【発明の実施の形態】上記構成によって、本発明の診断・治療装置は、光源の切り換え部を不要とすることができ、もって装置の小型化を図ることができるとともに、治療中の同時診断をも可能とすることができる。

【0019】以下、本発明の一実施の形態について図面を参照しながら説明する。図1は本実施の形態の診断・治療装置に用いられる医療用レーザー装置の構成を示すブロック図である。図1において、1は半導体レーザーで、0℃における動作時の発振波長が664nm、半値幅が±1nm、発振波長の温度特性が0.2nm/deg、動作可能温度範囲が-100～+80℃の特性を持っている。2は半導体レーザー1から出射されたレーザー光3を照射用レーザー光3aと波長検出用レーザー光3bに分岐する光学系、4は光ファイバ、5は病巣部Aとその周辺部Bを含む治療部位であらかじめ光感受性物質6が投与されて集積されている。7は制御手段、8は温度制御装置、9は波長検出用レーザー光3bの波長を検出する波長検出手段、10は波長表示手段、11はシャッターで制御手段7と協調し自動照射禁止手段を構成する。

【0020】以上のように構成された医療用レーザー装置についてその動作を説明する。半導体レーザー1が出射するレーザー光3の波長は、半導体レーザー1の温度によって決定する。すなわち、半導体レーザー1の温度を、温度制御装置8により-100～+80℃の範囲に可変制御することによってレーザー光3の波長を644～680nmの範囲で変化させることができる。これにより、使用する光感受性物質6の吸収波長と施術目的に適合した波長のレーザー光3を得ることができる。

【0021】本実施の形態では、光感受性物質6として（表1）のクロリン系のNPe6（商品名）を用いて吸収波長帯の中心波長664nmのレーザー光3を得るときは温度を0℃に、後述する目的で吸収波長帯の中で短波長側である660nmの波長をもつレーザー光3を得るときは温度を-15℃に制御した。また、フェオホルバイト系のPH-1126（商品名）を用いて同じく吸収波長帯の中心波長650nmのレーザー光3を得るときは温度を-70℃に、吸収波長帯の中で短波長側である644nmの波長をもつレーザー光3を得るときは温度を-100℃に制御した。

【0022】また、前記0℃、-20℃、-70℃および-100℃に温度制御したときに半導体レーザー1が出

射するレーザー光3の波長は、半値幅が±1nmであるからそれぞれ663～665nm、659～661nm、649～651nmおよび643～645nmで、レーザー光3のエネルギーは使用している光感受性物質6の吸収波長帯にあった。

【0023】このようにして温度を制御した半導体レーザー1より出射されるレーザー光3の一部は、光学系2により分岐されて波長検出用レーザー光3bとして波長検出手段9に導かれて所定の波長制御条件に適合しているかどうかを検出される。波長検出結果は波長表示手段10に表示されるとともに、適合状態でない場合には自動照射禁止手段が働き照射用レーザー光3aをシャッター11により遮断する。

【0024】レーザー光3が所定の波長制御条件に適合している場合にはシャッター11が開き照射用レーザー光3aは光ファイバ4に集光して照射され、光ファイバ4の先端から治療部位5に照射される。

【0025】以上のように本実施の形態によれば、レーザーの発振波長を制御して複数種類の光感受性物質の吸収波長と施術目的に適合し、半値幅の狭い波長をもつレーザー光を得ることができ、効率良く光感受性物質を励起することができる。また、メンテナンスもほとんど不要となり小型化および低価格化も実現できる。

【0026】次に診断・治療装置について、図面を参照しながら説明する。図2は本実施の形態における癌の診断・治療装置の構成を示すブロック図である。図2において、21はレーザー光源で、上記に説明した半導体レーザーを用いた医療用レーザー装置である。22はレーザー光源21からの照射用レーザー光3aを病巣部付近に導く光伝送路、23は病巣部およびその周辺を観察するための蛍光による画像伝送路で、24は光伝送路22および画像伝送路23を内蔵して病巣部付近に導く導光器である。25は撮像・解析手段で、画像伝送路23を通して得られる病巣部付近の画像を撮像して解析処理し、この結果は画像表示手段26に表示される。27は誘電体多層膜で構成された指定波長に対して±3nm程度の極めて狭いバンド幅のバンドパスフィルタ（たとえば、図3に示した特性をもつ日本真空光学株式会社の全誘電体干渉フィルターDIF型など）で、使用する光感受性物質の蛍光波長（クロリン系光感受性物質の場合約670nm、フェオホルバイト系光感受性物質の時は約654nm）付近の光だけを照射用レーザー光3aの波長と区別して透過することのできるもので、画像伝送路23と撮像・解析手段25を結ぶ光路上に配置されている。なおバンドパスフィルタ27は複数種類の光感受性物質にそれぞれ適応する複数種類のバンドパスフィルタを有しその切換え手段（図示せず）を備えている。なお、図2の治療部位5などの符号は図1と同様である。

【0027】以上のように構成された癌の診断・治療装置について、その動作を説明する。まず、レーザー光源2

1から出射される照射用レーザ光3aは光伝送路22を介して、あらかじめ光感受性物質を集積させた治療部位5に照射される。このとき、照射用レーザ光3aの波長は使用している光感受性物質に対応して治療効果が最適となる光感受性物質の吸収波長帯の中心波長となるよう温度制御装置を用いて制御する。すなわち、光感受性物質がクロリン系のNPe6の場合は664nm、フェオホルバイド系のPH-1126の場合は650nmに制御する。この波長制御の動作は既に記述した。

【0028】そして、治療部位5に照射用レーザ光3aが照射されると、あらかじめ集積させた光感受性物質の作用により病巣部Aが選択的に治療されるとともに、病巣部Aの光感受性物質が励起され前述した特定の波長の蛍光を発する。この蛍光による画像を撮像して解析することにより治療部位5の診断を行うが、この蛍光の波長は、照射用レーザ光3aの波長と近似しているうえ強度が弱いため、照射用レーザ光3aの散乱光の影響を強く受け画像の撮像と解析は一般には困難である。

【0029】しかし、この蛍光を画像伝送路23で導いた後、図3にその1例を示したような特性を持ち、使用している光感受性物質の発する蛍光の波長だけを透過して照射用レーザ光3aの波長を遮断するバンドパスフィルタ27を通すことにより、照射用レーザ光3aの散乱光の影響を排除して蛍光画像のみが撮像・解析手段25に入力される。撮像・解析手段25はこの蛍光による画像情報を撮像して解析処理し、その解析結果が画像表示手段26に表示される。この表示を観察することで治療中にも病巣部Aをリアルタイムで診断することができる。

【0030】蛍光(S)と照射用レーザ光3aの散乱光(N)の分離(S/N比)をより改善する目的で、照射用レーザ光3aの波長を蛍光の波長から離す方向にずらす制御を行うこともできる。すなわち、照射用レーザ光3aの波長を使用している光感受性物質の吸収波長帯の中心波長(例えば、NPe6の場合は664nm、PH-1126の場合は650nm)から、吸収波長帯の範囲で蛍光波長から遠ざかるよう(例えば、NPe6の場合は660nm、PH-1126の場合は644nm)にずらすように波長制御する。このように制御すると蛍光と照射用レーザ光3aの散乱光のS/N比が改善され、同時に実施例1ですでに説明したごとく照射用レーザ光3aのエネルギーは使用している光感受性物質の吸収波長帯にあり、治療効果の低下はほとんどない。

【0031】ここで述べたことを実現するために、特定の光感受性物質のみ(例えばNPe6またはPH-1126など)を使用する診断・治療装置にあってもレーザ光3の発振波長をその光感受性物質の有効吸収波長の範囲(例えばクロリン系のNPe6の場合は $664 \pm 5$ nm、またフェオホルバイト系のPH-1126の場合は $650 \pm 10$ nmなど)に可変とした。

【0032】また、本実施の形態における医療用レーザ装置は照射用レーザ光3aの波長を簡単に制御できるので、治療中の同時診断が不要になった場合には、照射用レーザ光3aの波長を治療に最適な光感受性物質の吸収波長帯の中心波長に戻すこともできる。また、本実施の形態における医療用レーザ装置は出射しているレーザ光3の波長値または波長制御条件に適合したかどうかが表示され、あるいは、レーザ光3の波長が波長制御条件に適合していないときはレーザ光は照射されないこともすでに述べた。

【0033】以上のように本実施の形態によれば、レーザ光により光感受性物質が発する蛍光の波長を透過し、レーザ光の波長を遮断するバンドパスフィルタを備えることにより、単一のレーザ光源で治療と診断ができる。また、波長制御手段がレーザ光の波長を、光感受性物質の吸収波長帯の中でこの光感受性物質が発する蛍光波長から遠ざかるようにずらすことにより、治療中の同時診断においても画像の安定したS/N比を確保することができる。

【0034】なお、上記説明において、レーザは半導体レーザとしたが、レーザはレーザ光の半値幅が狭く、レーザ光の発振波長が可変である他のレーザとしてもよい。また、半導体1は上記実施の形態にあげた特性を有するものに限定するものでないことは言うまでもない。

【0035】なおまた、本実施の形態では温度制御として波長検出手段9を用いてフィードバック制御を行う例を示したが、使用する半導体レーザの温度と発振波長の関係をあらかじめ記憶した記憶手段を備えて、この関係に基づいて半導体の温度を制御することによっても、正確な波長制御が可能である。

【0036】

【発明の効果】以上の説明から明らかなように、本発明の診断・治療装置は、光源の切り換え部を不要とすることができ、もって装置の小型化を図ることができる。また、治療中の同時診断をも可能とすることができる。

【図面の簡単な説明】

【図1】本発明の一実施の形態における医療用レーザ装置の構成を示すブロック図

【図2】本発明の一実施の形態における診断・治療装置の構成を示すブロック図

【図3】同診断・治療装置で使用したバンドパスフィルタの特性図

【図4】従来のレーザ装置を用いた癌の診断・治療装置の構成を示すブロック図

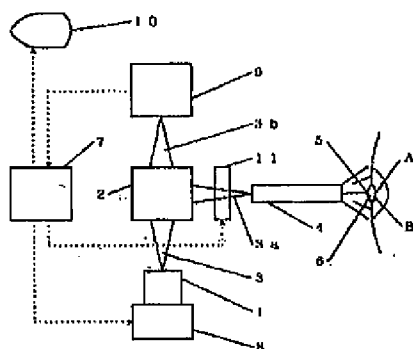
【符号の説明】

- 1 半導体レーザ(レーザ)
- 3 レーザ光
- 5 治療部位(病巣部)
- 6 光感受性物質
- 8 温度制御装置(波長制御手段)

- 21 レーザ光源（医療用レーザー装置）  
 22 光伝送路  
 23 画像伝送路

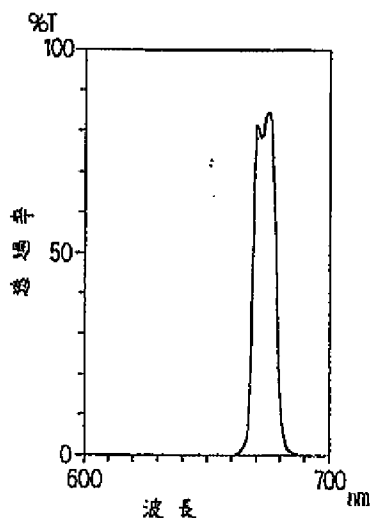
- 25 撮像・解析手段  
 26 画像表示手段  
 27 バンドパスフィルタ（蛍光分離手段）

【図1】

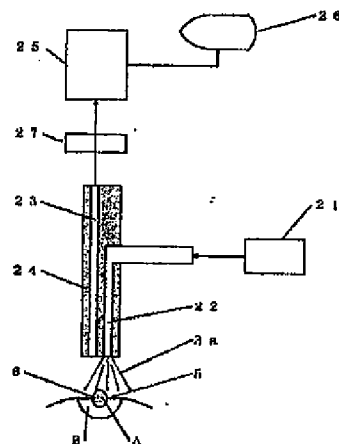


- 1 半導体レーザー（レーザー）  
 3 レーザ光  
 5 消滅層板  
 6 光感受性物質  
 8 温度制御装置（温度制御手段）

【図3】

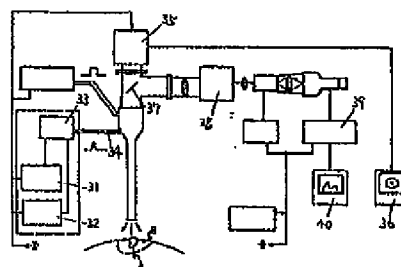


【図2】



- 21 レーザ光源（医療用レーザー装置）  
 22 光伝送路  
 23 画像伝送路  
 24 撮像・解析手段  
 25 温度制御手段  
 26 バンドパスフィルタ（蛍光分離手段）

【図4】



フロントページの続き

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